Incidence of ipsilateral postoperative deep venous thrombosis in the amputated lower extremity of patients with peripheral obstructive arterial disease

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Objective: **Patients undergoing amputation of the lower limb due to peripheral arterial disease (PAD) are at risk of developing deep venous thrombosis (DVT). Few studies in the research literature report the incidence of DVT during the early postoperative period or the risk factors for the development of DVT in the amputation stump. This prospective study evaluated the incidence of DVT during the first 35 postoperative days in patients who had undergone amputation of the lower extremity due to PAD and its relation to comorbidities and death.**

Methods: **Between September 2004 and March 2006, 56 patients (29 men), with a mean age of 67.25 years, underwent 62 amputations, comprising 36 below knee amputations (BKA) and 26 above knee amputations (AKA). Echo-Doppler scanning was performed preoperatively and on postoperative days 7 and 31 (approximately). All patients received acetylsalicylic acid (100 mg daily) preoperatively and postoperatively, but none received prophylactic anticoagulation.**

Results: **DVT occurred in 25.8% of extremities with amputations (10 AKA and 6 BKA). The cumulative incidence in the 35-day postoperative period was 28% (Kaplan-Meier). There was a significant difference ($P = .04$) in the incidence of DVT between AKA (37.5%) and BKA (21.2%). Age ≥70 years (48.9% vs 16.8%, $P = .021$) was also a risk factor for DVT in the univariate analysis. Of the 16 cases, 14 (87.5%) were diagnosed during outpatient care. The time to discharge after amputation was averaged 6.11 days in-hospital stay (range, 1-56 days). One symptomatic nonfatal pulmonary embolism occurred in a patient already diagnosed with DVT. There was no relation between other comorbidities and DVT. The multivariate analysis showed no association between risk factors and the occurrence of DVT in the amputated extremity. DVT ipsilateral to the amputation did not influence the mortality rate (9.7%).**

Conclusion: **The incidence of DVT in the early postoperative period (≤35 days) was elevated principally in patients aged ≥70 years and for AKA. Patients with PAD who have recently undergone major amputations should be considered at high risk for DVT, even after hospital discharge. Given the high rate of postoperative DVT observed in this study, we now recommend prophylactic anticoagulation for these patients, but further study is needed to determine the optimal duration and efficacy of this treatment. (J Vasc Surg 2008;48:1514-9.)**

Although many studies have considered venous thromboembolism (VTE) in clinical and surgical patients, few have focused on patients who have undergone amputation of the lower extremities because of peripheral arterial disease (PAD). To our knowledge, no prospective research studies with a sufficiently large amputee patient sample have considered the incidence of deep venous thrombosis (DVT) in the early postoperative period. Data from existing studies are divergent, and the incidence of VTE is highly variable, ranging from 0% to 66.66%.[1,2] Amputation involves considerable surgical trauma, including bone and soft tissue dissection and division, and many surgeons do not administer pharmacologic DVT prophylaxis because of concerns about bleeding complications.

Studies of patients undergoing hip and knee prosthesis procedures show a high incidence of DVT, not only in the early postoperative period but also up to 30 days after surgery.[3,4] Studies involving amputation of ischemic extremities have been limited to the hospitalization period and provide no data on the occurrence of DVT after discharge.[5-10]

In the present prospective study, we included patients with PAD who underwent major amputation of the lower extremity, and aimed to evaluate (1) the postoperative incidence of DVT in the amputated extremity during hospitalization and after discharge, (2) the relation between comorbidities and DVT incidence, and (3) the relation of DVT to symptomatic pulmonary embolism (PE) and operative mortality.

METHODS

A prospective and descriptive study of patients admitted consecutively to the Emergency Department and the Vascular Surgery Ward of the Clinics Hospital of the Faculty of Medicine of São Paulo University, Brazil, was conducted from September 2004 through March 2006. The study was reviewed and approved by the local Research Ethics Committee.

The following variables were studied: age, sex, heart disease, smoking, bedridden status, female hormone therapy, obesity (body mass index >30 kg/m^2), systemic arte-

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rial hypertension, diabetes mellitus, chronic renal failure, varicose veins of the lower extremities, paresthesia or paraplegia of the limbs, malignancy, level of arterial occlusion, secondary infection of the ischemic extremity, and recent arterial revascularization surgery. We analyzed the association between the incidence of VTE and the level of amputation, general medical postoperative complications, amputation stump complications, and postoperative mortality.

The accuracy of each patient's history and clinical examination was tested, comparing the data with color-flow Doppler findings, and checking clinical examination sensitivity and specificity.

Duplex ultrasound (DUS) scanning was chosen as the diagnostic method for DVT due to its noninvasive characteristic and ability to provide reproducible results in repeated examinations,[11] as well as its high sensitivity in examining the proximal deep venous system of the lower extremity.[12-14] Patients underwent DUS imaging once before amputation and twice after surgery, between postoperative days 3 and 15, and between days 16 and 35.

All examinations were performed using a Logiq 5 ultrasound system (GE Healthcare, Milwaukee, Wisc). The superficial femoral veins and common veins were examined, as well as the popliteal vein and saphenofemoral junction, for both lower extremities.[15] B-mode was used to detect intraluminal thrombi and vein compressibility, color mode was used to evaluate flow, and Doppler spectral mode was used for evaluation of the curve pattern. The examination included the iliac veins whenever alteration in respiratory flow phasicity was present in the common femoral vein. The examination result was considered positive for DVT when thrombus was identified and venous flow absent.[12,13,16]

All patients received acetylsalicylic acid (100 mg, daily) preoperatively and postoperatively, but none received prophylactic anticoagulation. Patients underwent stimulation for early mobilization combined with motor and respiratory physical therapy, and were referred to an outpatient rehabilitation center at discharge. Patients diagnosed with DVT were treated with nonfractionated heparin or low-molecular-weight heparin, followed by warfarin sodium for a period of 6 months.[14,17,18]

All patients investigated in the study presented with chronic arterial obstruction of the lower extremities, with or without previous arterial revascularization, and were indicated for above knee amputation (AKA) or below knee amputation (BKA). Patients who received any type of anticoagulation therapy before surgery or who were unwilling to participate in the study were not included. The treatment regimen in patients excluded due to previous anticoagulation was not discontinued.

Patients were excluded from the study if (1) DVT was identified during the preoperative or intraoperative period (all divided veins were assessed for the presence of intraluminal thrombi and the findings were reported by the surgeon), (2) the postoperative DUS scan was not performed for any reason, (3) DVT was diagnosed only in the contralateral extremity during the postoperative period, and (4) postoperative anticoagulation was administered for any reason (treatment or prophylaxis).

Table I. Patients excluded from the study and causes (n = 26)

Exclusion criteria	*No.*
Pre-op presence of DVT	6
Intra-op diagnosis of DVT	2
Contralateral DVT in post-op period	2
No post-op echo-Doppler (due to lack of conditions/death)	9
Post-op anticoagulant treatment	4
Complications of amputation stump with hip disarticulation	1
Lost to follow-up	2

DVT, Deep venous thrombosis.

Table II. Prevalence of associated diseases (n = 60)

Disease	*No. (%)*
Systemic arterial hypertension	48 (80.0)
Diabetes mellitus	42 (70.0)
Heart disease	16 (26.7)
Varicose veins of lower limbs	14 (23.3)
Cerebral vascular accident	13 (21.7)
Obesity	7 (11.7)

Statistical analysis. The cumulative incidence of DVT of the stump and mortality were determined by the Kaplan-Meier method, with an accepted standard error of up to 0.1. Univariate analysis of the risk factors for DVT was obtained by the log-rank test method, and Cox regression was applied for multivariate analysis. Statistical significance was set at $P < .05$.

RESULTS

During the study period, 82 patients with PAD underwent 88 amputations. As summarized in Table I, 26 patients were excluded from the study; thus, 62 amputations were studied in 56 patients, three of which were bilateral amputations. In three other patients, a new proximal amputation was performed 30 days after the first surgery. The mean age of the patients was 67.25 ± 11.7 years (range, 43-88 years), and 51.7% were men. The prevalence of associated diseases is listed in Table II. Of the 56 patients studied, 37 (66.0 %) were unable to walk before amputation, and 12 (21.4%) were smokers.

Six patients had prior amputations of contralateral limbs (4 BKA and 2 AKA), and two patients underwent bilateral BKA in the same surgery. In all cases the primary indication for amputation was critical limb ischemia associated with tissue necrosis. In 76.7% there was also an associated local infection. Eight patients (12.9%) had undergone an arterial revascularization in the previous 30-day period.

The predominant location of obstructive arterial disease in the amputated limb was the femoropopliteal segment (71%). The prevalence of both iliofemoral and infra-

Table III. Diseased venous segment and level of amputation

Venous segment	*Amputation level*		*Total*
	Above knee	*Below knee*	
Femoral	10	4	14
Popliteal	0	1	1
Femoropopliteal	0	1	1
Total	10	6	16

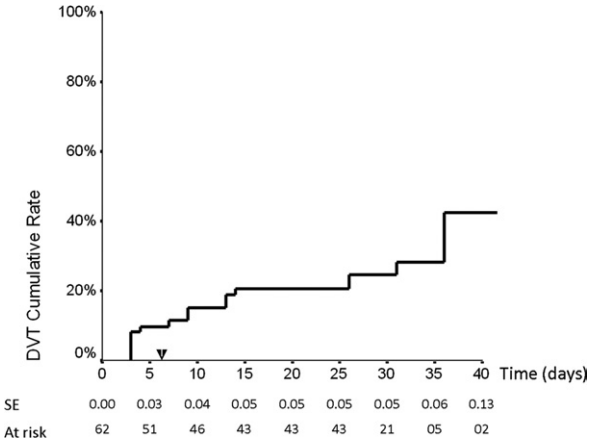

Fig 1. Cumulative incidence of venous thrombosis of the amputation stump by the Kaplan-Meier method. The *arrowhead* indicates the average day of discharge after amputation.[6,11]

popliteal disease was 14.5%. The most frequent level of amputation was BKA, in 36 (58.1%) cases. The left lower extremity was the site of amputation in 51.6%. None of the patients underwent knee disarticulation.

Mortality in the 30-day period was 9.7%. Most deaths had well-established causes, except for one patient in which autopsy presented no specific diagnosis (no evidence of PE).

Medical complications occurred in 20.0% of the patients as follows: bronchopneumonia in 11.7%, peritonitis and acute myocardial infarction in 3.3% each, and sepsis in 1.7%. One patient (1.6%) presented with a symptomatic nonfatal PE. Amputation stump complications occurred in 45.3% of the amputations. In five cases of BKA, an early (≤30 days) more proximal amputation was necessary.

During recovery, 16 cases of DVT were diagnosed in the ipsilateral amputated extremity (Table III), 12 within the first 15 days (75%) and four after this period. Of the 16 cases, 14 (87.5%) were diagnosed during outpatient care, the average time to discharge after amputation was 6.11 days (range, 1-56 days). No iliac DVT was diagnosed, and none of the patients who underwent bilateral amputation had evidence of DVT. DVT also occurred in the contralateral limb in three patients. The cumulative incidence of DVT ipsilateral to the amputation was 24.4% ≤30 days and 28.0% ≤35 days, with respective standard errors of 0.057 and 0.064 (Fig 1).

Table IV. Univariate analysis of risk factors for deep venous thrombosis of the amputation stump (log rank)

Factor	*No.*	*DVT per 100 individuals/d*	*Rate of events*	P
Sex				
Male	31	1.506	1	.13
Female	31	0.725	0.48	
Arterial hypertension				
Yes	50	1.063	0.95	.89
No	12	1.115	1	
Diabetes mellitus				
Yes	44	0.810	0.44	.09
No	18	1.837	1	
Smokers				
Yes	13	0.929	0.84	.69
No	49	1.112	1	
Bedridden				
Yes	39	0.819	0.53	.20
No	23	1.557	0	
Amputation level				
Thigh	26	1.792	1	.044
Leg	36	0.643	0.36	
Age, y				
≤69	36	0.590	0.28	.012
≥70	26	2.105	1	
Side				
Left	32	0.960	0.81	.55
Right	30	1.180	1	
Obesity				
Yes	8	0.885	0.62	.66
No	54	1.419	1	
Ischemia/limb infection				
Yes	48	1.025	0.83	.76
No	14	1.242	1	
Reamputation				
Yes	5	2.273	1	.66
No	57	1.036	0.46	
Contralateral amputation				
Yes	6	1.460	1	.67
No	56	1.033	0.71	
Stroke				
Yes	14	1.163	1	.94
No	48	1.045	0.90	
Heart disease				
Yes	17	1.626	1	.37
No	45	0.890	0.55	
Revascularization				
Yes	8	1.031	0.96	.99
No	54	1.078	1	
Stump complications				
Yes	27	1.250	1	.67
No	35	0.939	0.75	
Clinical complications				
Yes	11	0.725	0.63	.44
No	51	1.151	1	
Death				
Yes	6	3.278	1	.20
No	56	0.978	0.3	
Varicose veins				
Yes	15	1.312	1	.72
No	47	0.990	0.75	

DVT, Deep venous thrombosis.

Clinical evaluation of the signs and symptoms of DVT in the amputated limb had sensitivity of 56.2%, specificity 82.6%, negative-predictive value of 84.4%, and a positive-predictive value of 52.9%.

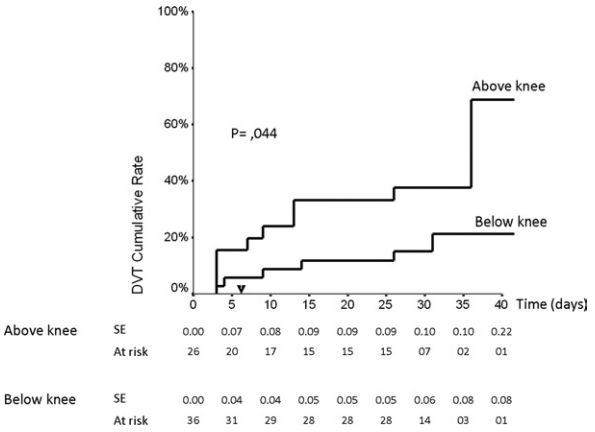

Fig 2. Cumulative incidence by long-rank analysis of venous thrombosis of amputation stump divided by amputation level above knee *(top line)* and below knee *(bottom line)*. The *arrowhead* indicates the average day of discharge after amputation.[6,11]

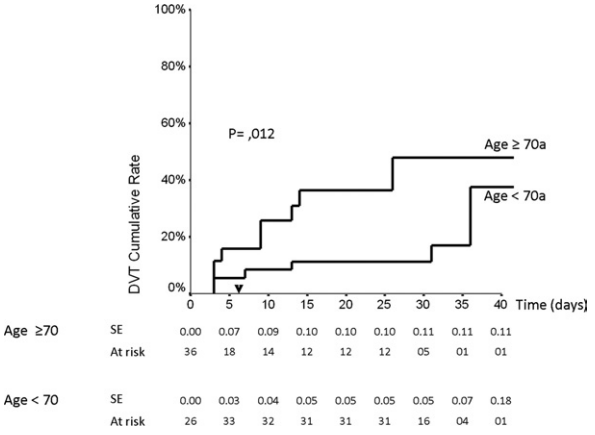

Fig 3. Cumulative incidence by log-rank analysis of venous thrombosis of the amputation stump divided by age ≥70 years *(top line)* and age <70 *(bottom line)*. The *arrowhead* indicates the average day of discharge after amputation.[6,11]

Univariate analysis (Table IV) demonstrated a significant difference in the incidence of DVT ipsilateral to the amputation when different levels were compared. AKA presented a cumulative incidence of venous thrombosis of 37.5%, compared with 21.2% in patients who underwent BKA, within the period up to day 35 after surgery ($P = .04$; Fig 2).

Patients aged ≥70 years had significantly higher risk for DVT in the amputated limb than younger patients within the 35-day period (48.9% vs 16.8%, respectively; $P = .012$; Fig 3). The multivariate analysis showed no association between risk factors and the occurrence of DVT in the amputated extremity.

DISCUSSION

Analysis of the general patient characteristics revealed no difference in the indications for amputation and complications in the amputated extremity with regard to previous related data.[19-23] The most frequent site of chronic arterial occlusion in this investigation was the superficial femoral artery, in accordance with Roon et al.[24] The percentage of patients who had undergone recent prior revascularization of the amputated limb was within the limits found in the literature.[25-28] We also observed that the concomitant bilateral amputations were in accordance with other reports that stated values of 10.68% to 15%.[23,29]

Previous studies[30,31] reported that failed BKA occurs in approximately 15% of patients, similar to the incidence observed in the present study. All new amputations to a more proximal level were performed in the BKA group. BKA failure was probably related to the surgery being performed distal to a femoropopliteal obstruction (absence of a palpable popliteal pulse) and close to an infection source. Most patients had combined ischemia and local infection preoperatively; these are contributing factors for infection as the major cause of BKA complication (54.5%). The occurrence of these complications and new amputation to a more proximal level did not influence the incidence of DVT.

Previous studies report that the incidence of nonfatal symptomatic PE varies from 2.1% to 8%.[23,24] We believe that the low incidence of symptomatic PE in the present study was due to the diagnostic accuracy of the DUS series, which resulted in immediate treatment of DVT and a consequent decrease in the incidence of PE. Another possible reason was our choice not to investigate patients without pulmonary symptoms. When diagnostic examinations were performed for routine asymptomatic PE in previous studies, results varied from 11% to 14.28%.[32,33] Although the study by Williams et al[34] attributed a PE risk four times higher for amputations at the AKA level, we had no cases of PE for AKA amputation in our study and only one PE in a BKA.

Previous reports described perioperative mortality for major amputation varying from 0% to 37%.[24,35-37] We also observed a mortality rate within this range. Univariate statistical analysis revealed no relationship between DVT and death. Nearly all DVT was diagnosed in the first 15 days after surgery, in agreement with previous studies, independent of sample and methodology used.[5-10]

The patients who required amputation were not solely at risk in the early postoperative period, they were also at risk after hospital discharge. In this study, 87.5% of the DVT diagnoses were made at the scheduled outpatient return appointment for the postoperative DUS examination. This finding differs from that of others studies because most researchers have studied the incidence of DVT only during the hospitalization.[1,2,5-7]

A relationship was found between the type of amputation performed and the incidence of DVT. The high incidence of DVT in patients who underwent AKA is probably because the femoral vein is a conduction vessel with few tributaries, a feature that leads to poor venous flow in its remnant segments and consequent thrombosis. Old age (≥70 years) was another factor related to

DVT ipsilateral to the amputation, but no difference was observed in the distribution of AKA and BKA, or bedridden individuals.

The presence of the other studied risk factors and variables showed no relation to DVT ipsilateral to the amputation, even after multivariate analysis; this finding is in contrast to data from previous studies for clinical and surgical patients in general.[38-47] This discrepancy may reflect the relatively small number of patients in the present study.

Yager et al[5] demonstrated DVT risk factors to be chronic venous insufficiency or previous history of DVT, or both, and the presence of prior amputation of the contralateral extremity. Their analysis also included patients diagnosed in the preoperative period (6 of 9, 66.7%) and in the contralateral limb (4 of 9, 44.4%), and was conducted using a methodology distinct from that used in our study, in which we only considered postoperative cases of DVT in the amputated extremity stump.

CONCLUSION

The incidence of DVT ipsilateral to the amputation is elevated during the early postoperative period (35 days), mainly in AKA and at ages of ≥70 years. There was no relationship between the presence of the other comorbidities studied and postoperative DVT occurrence. All patients with PAD scheduled to undergo major amputation should be considered at high risk for the development of DVT, even during the period after discharge from the hospital. On the basis of these results, we recommend prophylactic anticoagulation (if not contraindicated) and surveillance to all patients undergoing this type of procedure. Further studies are required to determine the optimal method and duration for prophylaxis treatment.

AUTHOR CONTRIBUTIONS

Conception and design: MM, CP, BM, PL
Analysis and interpretation: MM, CP, IC
Data collection: MM
Writing the article: MM, CP, IC
Critical revision of the article: BM, PL
Final approval of the article: MM, CP, IC, BM, PL
Statistical analysis: IC
Obtained funding: No funding
Overall responsibility: MM

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